IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF: Zheng Jane Li, *et al.*

APPLICATION NO.: 10/650,252

FILING DATE: August 27, 2003

TITLE: CRYSTAL FORMS OF AZITHROMYCIN

Examiner: Peselev, Elli

Group Art Unit: 1623

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

DECLARATION UNDER RULE §132

I, Zheng Jane Li, declare that:

1. I am an Associate Research Fellow in the Salt Selection and Crystallization Laboratory at Pfizer-Groton, CT. Since 1998, I have held the positions of Senior Research Scientist, Senior Principal Scientist and Associate Research Fellow at Pfizer, Inc. and have being working on crystallization of pharmaceutical materials.

2. I received my Bachelor of Science degree in chemical engineering from Beijing Polytechnic University in 1982, a Master of Science degree in Physical Chemistry from Michigan State University in 1984, and a Doctor of Philosophy in Pharmaceutics from University of Minnesota in 1996.

3. Prior to joining Pfizer, I did research work on pharmaceutical development for about 10 years. Through the course of my career as a scientist, I have developed expertise in solid-state pharmaceutics and have a number of publications and patents in the field of solid-state chemistry of pharmaceutical crystals.

4. During my employment at Pfizer, I have worked and supervised others in making and testing various crystal forms of azithromycin, including their preparation and characterization.

5. I characterized various mixtures of azithromycin monohydrate hemi-ethanol solvate and azithromycin dihydrate using ^{13}C solid state NMR. The results are shown in Exhibits 1, 2 and 3.

6. Exhibit 1 displays the ^{13}C solid state NMR spectra of azithromycin monohydrate hemi-ethanol solvate and azithromycin dihydrate. Exhibit 2 indicates that there is a linear correlation between the known and the predicted azithromycin dihydrate content in the mixture of azithromycin monohydrate hemi-ethanol solvate and azithromycin dihydrate. Exhibit 3 demonstrates the ^{13}C solid state NMR spectra of various mixtures of azithromycin monohydrate hemi-ethanol solvate and azithromycin dihydrate with decreasing intensity of α-carbon in ethanol as increasing the dihydrate content.

7. Based on the testing results as well as my experience in the preparation and characterization of azithromycin crystals, I am of the opinion that both azithromycin monohydrate hemi-ethanol solvate and azithromycin dihydrate retain their own distinctive crystal structures in the mixtures of azithromycin monohydrate hemi-ethanol solvate and azithromycin dihydrate, and the mixture can be quantified using ^{13}C solid state NMR.

8. I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the Untied States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

ZHENG JANE LI, Ph.D.

August 9, 2005
DATE

Exhibit 1. The NMR spectra of azithromycin monohydrate hemi-ethanol solvate and azithromycin dihydrate

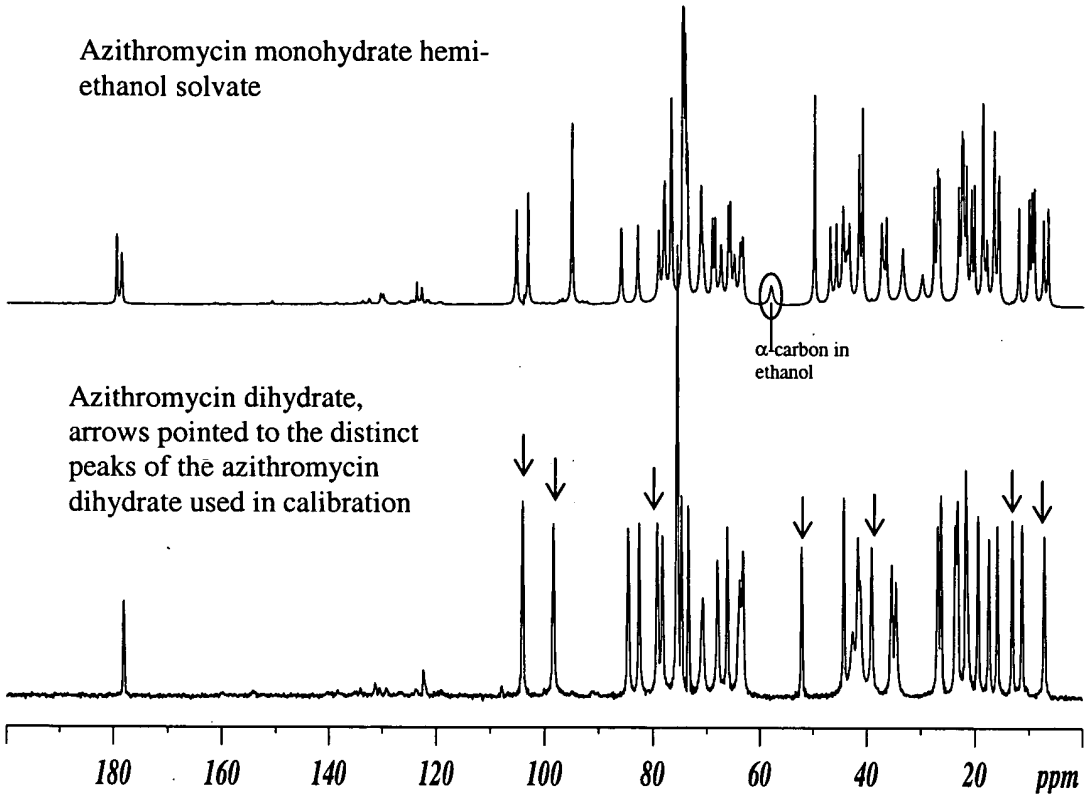

Exhibit 2. The correlation between the known and the predicted values for the percent of azithromycin dihydrate (labeled as %A) in the mixture of azithromycin dihydrate and azithromycin monohydrate hemi-ethanol solvate (R^2 value > 0.995)

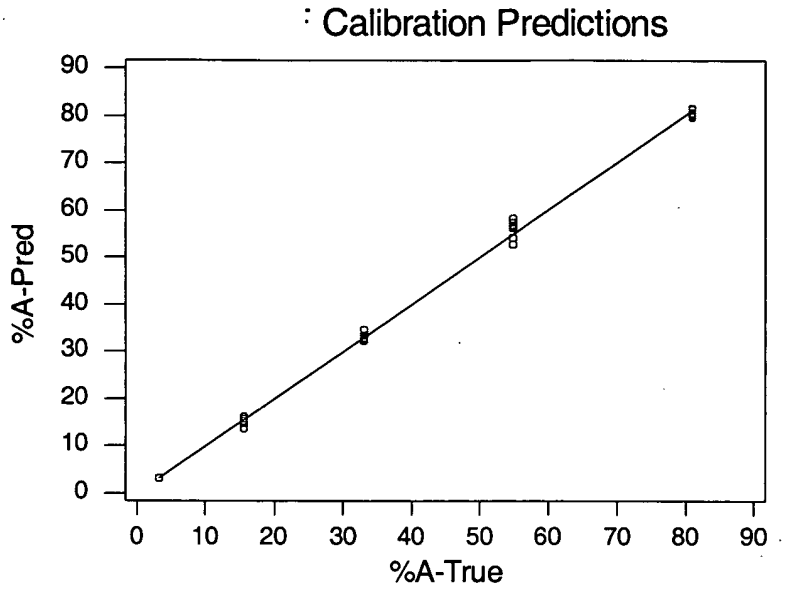

Exhibit 3. ^{13}C CPMAS NMR spectra of the mixtures of azithromycin dihydrate and azithromycin monohydrate hemi-ethanol solvate